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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/522,894	Applicant(s) SELVARAJ ET AL.	
	Examiner LI ZHENG	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 1-10, 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 February 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-19 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group II, claims 11-13, in the reply filed on 2/11/2008 is acknowledged.

Applicants request that claims 16-17 and claims 14-15 be considered together with the claims of Group II as they are linked by a single inventive feature, namely a RAFTIN hairpin construct and would not impose an undue burden (response, page 2, 1st and 2nd paragraphs).

Claims 14-17 have been rejoined with the claims of Group II.

Claims 1-10 and 18-19 are withdrawn for being drawn to non-elected invention.

Claims 11- 17 are examined on the merits.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.0. See, for example, pages 9 and 19.

4. The use of the trademarks "GenomeWalker™" has been noted in this application (page 21). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The specification is objected to for reciting "southern analysis" on page 7, line 31. Replacing the recitation with "'Southern analysis" is requested.

6. The specification is objected to under 37 CFR 1.821(d) as failing to refer to a sequence by use of its sequence identifier preceded by "SEQ ID NO:". The nucleotide sequences in Figure 4 should be identified by SEQ ID NOs. Alternatively, the brief descriptions of this figure on page 4 can be amended to recite the identifiers.

Claim Objections

7. Claim 11, line 1, is objected to for not reciting the article "a" before "sense".

Claim Rejections - 35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an RNA hairpin construct comprising a promoter operably linked to sense-oriented RAFTIN nucleotide sequence, an intron and an antisense-oriented RAFTIN nucleotide sequence.

The specification teaches isolation and characterization of the RAFTIN1 group of anther-tapetum specific genes, taRAFTIN1a, taRAFTIN1b and taRAFTIN1d in wheat and osRAFTIN1 in rice (page14, lines 18-21). Further BLASTX search of public gene database identify 12 ESTs from wheat, rice, barley, rye, sorghum and maize (the paragraph bridging pages 9-10).

First, the specification only describes RAFTIN1 gene, not RAFTIN gene as claimed.

The Applicants do not identify essential regions of the RAFTIN1. The only protein sequences described are taRAFTIN1a, taRAFTIN1b and taRAFTIN1d in wheat and osRAFTIN1 in rice. Although the specification identifies C-terminal moiety of RAFTIN1 sharing extensive homology to a BURP domain, such BURP domain is present in many other genes unrelated to RAFTIN1 group of genes (the paragraph bridging pages 16-17). There is no indication about the functional importance of this motif correlating to RAFTIN1 gene function.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of nucleotide sequences encoding the proteins falling within the scope of the claimed genus of polynucleotides encoding RAFTIN. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for RAFTIN1, it remains unclear what features identify a protein of RAFTIN1. Since said genus has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Scope of Enablement

9. Claim 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an RNA hairpin construct comprising a promoter operably linked to sense-oriented RAFTIN nucleotide sequence, an intron and an antisense-oriented RAFTIN nucleotide sequence, wherein RAFTIN is taRAFTIN1a in wheat, or osRAFTIN1 in rice, and wherein sense-oriented and antisense RAFTIN nucleotide sequences are at least 23 nucleotide sequences in length, as well as a transgenic rice plant comprising a plant transformation vector encoding said RNA hairpin construct, does not reasonably provide enablement for said RNA hairpin construct wherein the RAFTIN is any RAFTIN sequence with any length, or any transgenic plant or cells comprising said plant transformation vector. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The instant claims are broadly drawn to an RNA hairpin construct comprising a promoter operably linked to sense-oriented RAFTIN nucleotide sequence, an intron and an antisense-oriented RAFTIN nucleotide sequence, a transgenic plant, plant cell or seed comprising a transformation vector encoding the RNA hairpin construct, as well as a method for producing a plant having male sterility or modulated male fertility by transforming the transformation vector into plant cell.

The specification teaches isolation and characterization of the RAFTIN1 group of anther-tapetum specific genes, taRAFTIN1a, taRAFTIN1b and taRAFTIN1d in wheat and osRAFTIN1 in rice (page14, lines 18-21). Further BLASTX search of public gene database identify 12 ESTs from wheat, rice, barley, rye, sorghum and maize (the paragraph bridging pages 9-10). The specification further teaches that intron-spliced hairpin RNA using sense and antisense sequences of osRAFTIN1 or taRAFTIN1a

effectively reduces osRAFTIN1 expression in rice (Figure 7; also page 12, lines 3-25) and that down-regulation of osRAFTIN1 reduces male sterility in the transgenic rice (the paragraph bridging pages 12-13).

The specification fails to provide guidance on full length sequence information about RAFTIN gene family except for four members of RAFTIN1 gene family from wheat and rice. Gene silencing construct of instant invention requires sequence information about the RAFTIN1 gene(s) in a given plant. The instant invention claims generating any male sterile plant using any RAFTIN gene, whereas the specification only provide sequence information about four members of RAFTIN1 gene family from wheat and rice and only generate male sterile rice plant in which only one copy of RAFTIN gene is found. Further, the specification also fails to provide guidance on how to produce male sterile plant when there are multiple copies of RAFTIN genes in a plant. For example, the specification does not provide guidance on how to use plant or seed comprising dsRNA structure targeting taRAFTIN1b or taRAFTIN1d.

Still further, Thomas et al. (2001, *The Plant Journal* 25(4):417-425) teach that the lower size limit required for targeting reporter transgene mRNA de novo using PTGS was 23 nucleotides of complete identity, a size corresponding to that of small RNAs associated with PTGS in plant and RNAi in animals. Therefore, all of the DNA segments smaller than 23 nucleotides in instant claims are not enabled for silencing a target gene.

Therefore, in the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of known

Art Unit: 1638

NAFTIN1 genes as probes or by designing primers to undisclosed regions of known NAFTIN1 genes and isolating or amplifying fragments, subcloning the fragments, confirming copy number of NAFTIN gene in the plant, producing plant transformation vectors encoding RNA hairpin construct of NAFTIN1 and transforming plants therewith, in order to identify those, if any, that when expressed have reduced expression of NAFTIN1 genes and exhibit a male sterility phenotype. See *Genentech Inc. v. Novo Nordisk*, A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would be required for a person skilled in the art to practice the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Smith et al (2000, *Nature*, 407:319-320) in view of Sasaki et al (1999, Genbank Accession Number AP000364).

The instant claims are broadly drawn to an RNA hairpin construct comprising a promoter operably linked to sense-oriented RAFTIN nucleotide sequence, an intron and an antisense-oriented RAFTIN nucleotide sequence, a transgenic plant, plant cell or seed comprising a transformation vector encoding the RNA hairpin construct, as well as a method for producing a plant having male sterility or modulated male fertility by transforming the transformation vector into plant cell.

Smith et al teach that a DNA construct that produces hairpin loop type of dsRNA (hpRNA) with functional (i.e. spliceable) intron as spacer enhances silencing efficiency (last two paragraphs on left col. of page 320, and also figure 1). Smith et al. also teach that the modifications that help to align the complementary arms of the hairpin and promote the formation of a duplex could increase the efficiency of gene silencing (see last paragraph on the left column of page 320).

Smith et al. do not teach RAFTIN genes and RAFTIN promoter. Smith et al. does not teach a method for producing a plant having male sterility or modulated male fertility as well as the plant or seed produced by the method.

Sasaki et al. teach that a nucleotide sequence encoding a rice RAFTIN orthologue including coding region and promoter region.

Given the recognition of those of ordinary skill in the art of the value of studying gene function by reduce the expression of gene using dsRNA hairpin construct as taught by Smith et al., it would have been obvious for a person with ordinary skill in the

Art Unit: 1638

art to modify the hairpin construct of Smith et al. by replacing the FAD2 sense and antisense sequences with rice RAFTIN sense and antisense sequences of Sasaki et al., resulting in the instant invention. One skilled in the art would have been motivated to do so given the teaching of Smith et al. that such construct helps to align the complementary arms of the hairpin and promote the formation of a duplex could increase the efficiency of gene silencing (see last paragraph on the left column of page 320) and studying the gene function of a rice RAFTIN orthologue is highly desirable.

It would also have been obvious to use rice RAFTIN promoter of Sasaki et al. to replace the CaMV 35S promoter of Smith et al. given that using its own promoter would allow dsRNA of RAFTIN1 to be produced in the same stage as RAFTIN1 mRNA.

Although the combined teaching does not teach a method for producing a plant having male sterility or modulated male fertility, the method of combined teaching teach every step recited in the instant method. Therefore, the method of combined teaching would be obviously used for producing a plant having male sterility or modulated male fertility.

Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stuart F. Baum/
Primary Examiner, Art Unit 1638